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(54) Title: THERAPEUTIC COMPOSITIONS BASED ON EXTRACTS OF PLANTS FROM THE GENUS PLUMERIA (FRANGIPANI)

(57) Abstract: A therapeutic composition for topical use comprising an extract from a plant of the genus Plumeria. The composition can be used for preventing and treating skin cancers, fungal infections, viral infections and haemorrhoids. The composition can also be used for repairing and preventing defects of the skin.

THERAPEUTIC COMPSITIONS BASED ON EXTRACTS OF PLANTS FROM THE GENUS PLUMERIA (FRANGLPANI)

Field of the Invention

This invention relates to therapeutic compositions and methods of treatment utilising extracts of plants from the genus *Plumeria*. In particular, the invention relates to compositions and methods for treating skin cancers, fungal infections, viral infections, defects of the skin as well as other disorders.

Background of the Invention

Plants of the genus *Plumeria* (also known as *Plumiera*, common name Frangipani) are found throughout tropical and sub-tropical regions of the world. Species of *Plumeria* include *P. rubra, P. acutifolia, P. obtusa, P. obtusifolia, P. alba, P. bicolor, P. tricolour* and *P. jamesoni*.

Various uses for *Plumeria* have been described. The specification of GB 2 104 383 describes anti-fouling compositions prepared from *Plumeria*, for use as algicides and barnicides in paints. Hamburger et al (*J. Ethnopharmacol.* 1991 Jul; 33(3):289-92) describe bioactive compounds prepared from *P. rubra* having molluscicidal, cytotoxic and anti-bacterial activities. Extracts of the flowers of *Plumeria* have also been used as fragrances in cosmetics.

Summary of the Invention

The present inventor has discovered that extracts of *Plumeria* also have therapeutic properties and can be used in the prevention or treatment of skin cancers, fungal infections, viral infections, various skin defects and other afflictions.

According to a first aspect of the present invention, there is provided a composition for preventing or treating skin cancer, said composition comprising an extract from a plant of the genus *Plumeria*.

According to a second aspect of the present invention, there is provided a method for preventing or treating skin cancer in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

According to a third aspect of the present invention, there is provided the use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of skin cancer in a subject.

According to a fourth aspect of the present invention, there is provided a composition for preventing or treating a fungal infection, said composition comprising an extract from a plant of the genus *Plumeria*.

According to a fifth aspect of the present invention, there is provided a method for preventing or treating a fungal infection in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

According to a sixth aspect of the present invention, there is provided the use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of a fungal infection in a subject.

According to a seventh aspect of the present invention, there is provided a composition for preventing or treating a viral infection, said composition comprising an extract from a plant of the genus *Plumeria*.

According to an eighth aspect of the present invention, there is provided a method for preventing or treating a viral infection in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

According to a ninth aspect of the present invention, there is provided the use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of a viral infection in a subject.

According to a tenth aspect of the present invention, there is provided a composition for repairing or preventing a defect of the skin, said composition comprising an extract from a plant of the genus *Plumeria*.

According to an eleventh aspect of the present invention, there is provided a method of repairing or preventing a defect of the skin in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

According to a twelfth aspect of the present invention, there is provided the use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for repairing or preventing a defect of the skin in a subject.

According to a thirteenth aspect of the present invention, there is provided a composition for preventing or treating haemorrhoids, said composition comprising an extract from a plant of the genus *Plumeria*.

According to a fourteenth aspect of the present invention, there is provided a method of preventing or treating haemorrhoids in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

According to a fifteenth aspect of the present invention, there is provided the use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for preventing or treating haemorrhoids in a subject.

According to a sixteenth aspect of the present invention, there is provided a method for preparing a composition comprising an extract from a plant of the genus *Plumeria*, the composition being as described in other aspects of the invention.

Detailed Description of the Invention

Other aspects and embodiments of the invention will become apparent from the following detailed description thereof.

The present inventor has discovered that extracts of plants of the genus *Plumeria* have anti-cancer, antifungal and anti-viral activities as well as other therapeutic properties. Although the extract may be derived from any suitable species of the *Plumeria* genus (including *P. rubra, P. acutifolia, P.*

obtusa, P. obtusifolia, P. alba, P. bicolor, P. tricolour and P. jamesoni), deciduous forms of *Plumeria* are preferred as they appear to have the highest activities. Preferably, the extract is derived from *P. rubra*.

The extract can be prepared from any suitable part or parts of the plant. The extract can be prepared, for instance, from the branches, leaves, trunk, bark, milky sap (latex), flowers or roots of the plant. Preferably, the extract comprises milky sap collected from actively growing branches of the plant. Milky sap is exuded from the branches when bruised, cut or punctured. If necessary, the sap can be processed or stabilised in any suitable way.

With regard to the first, second and third aspects of the invention, the composition can be used to prevent or treat any suitable type of skin cancer. The composition can, for instance, be used to prevent or treat squamous cell carcinoma, basal cell carcinoma, melanoma, Kaposi's sarcoma, cutaneous lymphoma, adnexal tumour and Merkel cell carcinoma. The composition can also be used to prevent or treat precursors of skin cancer such as solar keratoses.

With regard to the fourth, fifth and sixth aspects of the invention, the composition can be used to prevent or treat any suitable type of fungal infection. Preferably, the composition is used to prevent or treat tinea (e.g. athlete's foot, jock itch, ringworm, deep nail bed infection) which is caused chiefly by species of *Microsporum, Trichophyton, Candida* and *Epidermophyton*.

With regard to the seventh, eighth and ninth aspects of the invention, the composition can be used to prevent or treat any suitable type of viral infection. Preferably, the composition is applied to sores, ulcers, lesions, blisters, cancers, inflammations, skin discolorations and other skin defects that are caused by a virus. Some of these are caused, for example, by herpes simplex virus 1 or 2 which primarily affect the mouth and genital areas. Human papillomavirus may cause carcinomas in genital areas.

With regard to the tenth, eleventh and twelfth aspects of the invention, the composition can be used to prevent or treat any suitable defect of the skin. The skin defect may be, for example, an age spot, a benign tumour, a blister, a burn, chicken pox, a cold sore, a crack, cradle cap, dermatitis,

diaper rash, eczema, a lesion, a mole, a papule, a pustule, a reddened area, rosacea, scaling, a stomatitis, an ulcer, a wound, or seborrhoeic keratosis.

Each composition described above can be formulated as a pharmaceutical or a cosmeceutical. Each composition can be administered to the subject in any suitable form in any suitable way. Preferably, the subject is a human or other mammal.

Each composition can be, for instance, administered topically in the form of a cream, foam, gel, milk, lotion, oil, ointment, paste, powder or solution. The compound can be incorporated into a bandage or plaster. Preferably, each composition is applied topically as a cream at least once, but preferably twice, a day.

Each composition of the present invention can include one or more other active ingredients. An active ingredient, as defined herein, is a compound that provides therapeutic benefit to the subject. The active ingredient can be, for instance, an antibiotic, antifungal, anti-inflammatory, anti-viral or wound healer. Salicylic acid and paraffin are examples of such ingredients.

Preferably, the composition further comprises the active ingredients benzoic acid and salicylic acid. Although these ingredients have been used topically as an antifungal and keratolytic agent in the treatment of tinea pedis (commercially available as Whitfield's Ointment™), the inventor has found synergy between the plant extract and one or more of the ingredients so as to more efficiently treat fungal infections.

Each composition of the present invention can further include one or more of the following types of ingredients: an adhesive, a base, a buffer, a carrier, a colourant, a diluent, a dispersing agent, an emollient, an emulsifier, an excipient, a flexibiliser/plasticiser, fragrance, a gelling agent, a humectant, an insecticidal agent, a lubricant, a preservative, a skin conditioning agent, a skin protectant, a solubiliser, a stabilising agent, a sunscreen agent, a surfactant, a suspending agent, a textural modifier, a thickening agent, a viscosity increasing agent, and a waterproofing agent.

Suitable organic, oily or aqueous bases, carriers, diluents and excipients are inert and physiologically acceptable and include, for example: bacteriostatic saline (saline containing benzyl

alcohol), cetomacrogol, cetyl alcohol, glycerine, lanolin, petrolatum based creams, gels, saline, short chain alcohols and glycols (e.g. ethyl alcohol and propylene glycol), and water.

An emollient can help skin maintain a soft, smooth and pliable appearance. The emollient can be, for example: acetyl arginine, acetylated lanolin, algae extract, almond oil, apricot kernel oil PEG-6 esters, avocado oil PEG-11 esters, bis-PEG-4 dimethicone, butoxyethyl stearate, C_{18}-C_{36} acid glycol ester, C_2-C_{13} alkyl lactate, caprylyl glycol, cetyl alcohol, cetyl esters, cetyl laurate, coconut oil PEG-10 esters, crodamol GTCC, di- C_{12}-C_{13} alkyl tartrate, diethyl sebacate, dihydrocholesteryl butyrate, dimethiconol, dimyristyl tartrate, disteareth-5 lauroyl glutamate, ethyl avocadate, ethylhexyl myristate, fatty alcohol, glyceryl isostearates, glyceryl oleate, hexyldecyl stearate, hexyl isostearate, hydrogenated palm glycerides, hydrogenated soy glycerides, hydrogenated tallow glycerides, hydroxypropyl bisisostearamide MEA, isostearyl neopentanoate, isostearyl palmitate, isotridecyl isononanoate, laureth-2 acetate, lauryl polyglyceryl-6 cetearyl glycol ether, macadamia nut oil, methyl gluceth-20 benzoate, mineral oil, myreth-3 palmitate, octyldecanol, octyldodecanol, odontella aurita oil, 2-oleamido-1, 3 octadecanediol, palm glycerides, PEG avocado glycerides, PEG castor oil, PEG-22/dodecyl glycol copolymer, PEG shorea butter glycerides, phytol, raffinose, shea butter, silicone 200/350, stearyl citrate, sunflower seed oil glycerides, and tocopheryl glucoside.

Either water in oil or oil in water emulsions can be used. Examples of suitable surfactants and emulsifying agents include: non-ionic ethoxylated and non-ethoxylated surfactants, abietic acid, almond oil PEG, beeswax, butylglucoside caprate, C_{18}-C_{36} acid glycol ester, C_9-C_{15} alkyl phosphate, caprylic/capric triglyceride PEG-4 esters, cetomacrogol, ceteareth-7, cetereth-20, cetyl phosphate, cetyl stearyl alcohol, corn oil PEG esters, DEA-cetyl phosphate, dextrin laurate, dilaureth-7 citrate, dimyristyl phosphate, glycereth-17 cocoate, glyceryl erucate, glycerol, glyceryl laurate, G.M.S. acid stable, hydrogenated castor oil PEG esters, isosteareth-11 carboxylic acid, lecithin, lysolecithin, nonoxynol-9, octyldodeceth-20, palm glyceride, PEG diisostearate, PEG stearamine, poloxamines, polyglyceryls, potassium linoleate, PPGs, raffinose myristate, sodium caproyl lactylate, sodium caprylate, sodium cocoate, sodium isostearate, sodium tocopheryl phosphate, steareths, TEA-C_{12}-C_{13} pareth-3 sulfate, tri-C_{12}-C_{15} pareth-6 phosphate, and trideceths.

A humectant can help maintain moisture levels in skin. The humectant can be for example: acetyl arginine, algae extract, aloe barbadensis leaf extract, betaine, 2, 3-butanediol, chitosan lauroyl glycinate, diglycereth-7 malate, diglycerin, diglycol guanidine succinate, erythritol, fructose, glucose, glycerine, honey, hydrolyzed wheat protein/PEG-20 acetate copolymer, hydroxypropyltrimonium hyaluronate, inositol, lactitol, maltitol, maltose, mannitol, mannose, methoxy PEG, myristamidobutyl guanidine acetate, polyglyceryl sorbitol, potassium PCA, propylene glycol, sodium PCA, sorbitol, sucrose, and urea.

Each composition can include one or more types of preservative. A suitable preservative, for example, can be: benzalkonium chloride, benzoic acid, benzothonium chloride, benzyl alcohol, 2-bromo-2-nitropropane-1,3-diol, bronopol, butylated hydroxyanisole, butylated hydroxytoluene, butyl paraben, chlorophene, chlorphenesin, diazolidinyl urea, DMDM hydantoin, ethyl paraben, formaldehyde-releasing preservative, hydroquinone, iodopropynyl butylcarbamate, imidazolidinyl urea, methyldibromo glutaronitrile, methylhydroquinone, methylisothiazolinone, methyl paraben, nitrosamines, o-cymen-5-ol, phenoxyethanol, propyl paraben, quaternium-15, sodium benzoate, sodium dehydroacetate, sodium hydroxymethylglycinate, sodium metabisulfite, and sodium sulfite.

A skin conditioning agent, as defined herein, improves dry or damaged skin. Such agents, for example, include: acetyl cysteine, N-acetyl dihydrosphingosine, acrylates/behenyl acrylate/dimethicone acrylate copolymer, adenosine, adenosine cyclic phosphate, adensosine phosphate, adenosine triphosphate, alanine, albumen, algae extract, allantoin and deriviatives, aloe barbadensis extracts, aluminum PCA, amyloglucosidase, arbutin, arginine, azulene, bromelain, buttermilk powder, butylene glycol, caffeine, calcium gluconate, capsaicin, carbocysteine, carnosine, beta-carotene, casein, catalase, cephalins, ceramides, chamomilla recutita (matricaria) flower extract, cholecalciferol, cholesteryl esters, coco-betaine, coenzyme A, corn starch modified, crystallins, cycloethoxymethicone, cysteine DNA, cytochrome C, darutoside, dextran sulfate, dimethicone copolyols, dimethylsilanol hyaluronate, DNA, elastin, elastin amino acids, epidermal growth factor, ergocalciferol, ergosterol, ethylhexyl PCA, fibronectin, folic acid, gelatin, gliadin, beta-glucan, glucose, glycine, glycogen, glycolipids, glycoproteins, glycosaminoglycans, glycosphingolipids, horseradish peroxidase, hydrogenated proteins, hydrolyzed proteins, jojoba oil, keratin, keratin amino acids, kinetin, lactoferrin, lanosterol, lauryl PCA, lecithin, linoleic acid, linolenic acid, lipase, lysine, lysozyme, malt extract, maltodextrin, melanin, methionine, mineral

salts, niacin, niacinamide, oat amino acids, oryzanol, palmitoyl hydrolyzed proteins, pancreatin, papain, PEG, pepsin, phospholipids, phytosterols, placental enzymes, placental lipids, pyridoxal 5-phosphate, quercetin, resorcinol acetate, riboflavin, RNA, saccharomyces lysate extract, silk amino acids, sphingolipids, stearamidopropyl betaine, stearyl palmitate, tocopherol, tocopheryl acetate, tocopheryl linoleate, ubiquinone, *vitis vinifera* (grape) seed oil, wheat amino acids, xanthan gum, and zinc gluconate.

A skin protectant, as defined herein, protects injured or exposed skin or mucous membrane surfaces from harmful or irritating chemicals. A skin protectant, for example, includes: algae extract, allantoin, aluminium hydroxide, aluminium sulfate, betaine, camellia sinensis leaf extract, cerebrosides, dimethicone, glucuronolactone, glycerin, kaolin, lanolin, malt extract, mineral oil, petrolatum, potassium gluconate, and talc.

The sunscreen agent can absorb, reflect or scatter UV radiation in the wavelength range of about 290 to 400 nanometers. Such agents include: benzophenone-3 (oxybenzone), benzophenone-4 (sulisobenzone), benzophenone-8 (dioxybenzone), butyl methoxydibenzoylmethane (Avobenzone), DEA-methoxycinnamate (diethanolamine methoxycinnamate), ethyl dihydroxypropyl PABA (ethyl 4- [bis (hydroxypropyl)] aminobenzoate), ethylhexyl dimethyl PABA (Padimate O), ethylhexyl methoxycinnamate (octyl methoxycinnamate), ethylhexyl salicylate (octyl salicylate), homosalate, menthyl anthranilate (Meradimate), octocrylene, PABA (aminobenzoic acid), phenylbenzimidazole sulfonic acid (Ensulizole), TEA-salicylate (trolamine salicylate), titanium dioxide, and zinc oxide.

Examples of thickening or viscosity increasing agents include: acrylamides copolymer, agarose, amylopectin, bentonite, calcium alginate, calcium carboxymethyl cellulose, carbomer, carboxymethyl chitin, castor oil derivatives, cellulose gum, cellulosic preparation, cetyl alcohol, cetostearyl alcohol, coconut oil, dextrin, gelatin, hydrogenated tallow, hydroxyethylcellulose, hydroxypropylcellulose, hydroxpropyl starch, inorganic thixotrope, magnesium alginate, methylcellulose, microcrystalline cellulose, modified clays, paraffin, pectin, various PEG's, polyacrylic acid, polymethacrylic acid, polyvinyl alcohol, quaternium ammonium compound of bentonite or zinc stearate, shea butter, various PPG's, sodium acrylates copolymer, sodium carrageenan, silicon dioxide, xanthum gum, and yeast beta-glucan.

Preferably, each composition comprises about 25% volume/volume sap from a plant of the genus *Plumeria* in an organic base or in an emulsion base.

Preferably, each composition comprises:
about 25% volume/volume sap from a plant of the genus *Plumeria*; and
a base having about 15% volume/volume Whitfield's Ointment™ pre-mixed with about 60% volume/volume either Vitamin E Cream or Sorbelene Cream. Preferably, the base has a low alcohol content.

Whitfield's Ointment™ can comprise 3 g/50 g benzoic acid and 1.5 g/50 g salicylic acid in a lanolin, petroleum jelly or other type of organic base. Whitfield's Ointment™ can be as manufactured by Gilseal Coy, Queensland, Australia or Biotech Pharmaceuticals, Queensland, Australia.

Vitamin E Cream can comprise tocopheryl acetate in an oily base. Vitamin E Cream can be as manufactured by Liberty Cosmetics, New South Wales, Australia.

Sorbelene Cream (being an emulsion) can comprise water, glycerine, cetamacrogol, liquid paraffin, cetyl stearyl alcohol, methyl paraben, propyl paraben and imidazolindinyl urea as manufactured by Amcal Chemists Ltd, Victoria, Australia, Jean Charles Professional Products, New South Wales, Australia or Lustra Labs., Victoria, Australia.

Preferred Embodiments of the Invention

Having broadly described the invention in its various aspects, non-limiting examples of embodiments will now be given.

Example 1

Preparation of a Cream Comprising a *Plumeria* Extract

This example describes the preparation of a therapeutic cream comprising an extract of *Plumeria rubra*.

A green-tipped branch of a *Plumeria rubra* plant was punctured with a knife and 12-20 drops of the milky sap (latex) of the plant were collected in a container. Within about three minutes of collecting the sap, the sap was mixed with a base comprising about 15% volume/volume Whitfield's Ointment™ (manufactured by Gilseal Coy, Queensland, Australia or Biotech Pharmaceuticals, Queensland, Australia) pre-mixed with about 60% volume/volume either Vitamin E Cream (manufactured by Liberty Cosmetics, New South Wales, Australia) or Sorbelene Cream (manufactured by Amcal Chemists Ltd, Victoria, Australia, Jean Charles Professional Products, New South Wales, Australia or Lustra Labs., Victoria, Australia). The volume of sap in the cream composition was about 25%.

Whitfield's Ointment™ typically comprises 3 g/50 g benzoic acid and 1.5 g/50 g salicylic acid in a lanolin or petroleum jelly (organic) base.

Vitamin E Cream typically comprises tocopheryl acetate in an oily base.

Sorbelene Cream (being an emulsion) typically comprises water, glycerine, cetamacrogol, liquid paraffin, cetyl stearyl alcohol, methyl paraben, propyl paraben and imidazolindinyl urea.

Since the latex separates/coagulates on exposure to air, the latex should be mixed with the base as soon as possible. One way of checking to see that there is sufficient latex in the composition is to place some of the composition between the forefinger and thumb. If there is insufficient latex in the composition, many fine latex-derived strands will not be evident when moving the thumb and forefinger away from one another.

Example 2

Anti-Cancer Treatment

The cream as described in Example 1 has been proven effective for the treatment of various cancers and pre-cancers, including: tumours of advanced breast cancer, viral penile carcinoma, squamous cell carcinoma (nose, hand, chest, vagina, leg), melanoma (ear, back, chest, neck, face), solar keratoses (hand, nose) and basal cell carcinoma (ear, face, arm, leg).

The cream was applied to the skin cancer or cancer precursor once or twice a day. No adverse

reactions were reported, the cream did not irritate the skin nor did it inflame the skin. On average, melanomas disappeared and were replaced by new healthy skin usually within three weeks. Solar keratoses, on average, disappeared and were replaced by new healthy skin usually within 10 days. On average, squamous cell carcinomas disappeared and were replaced by new healthy skin usually within two weeks.

Cancers have also been treated on the lower eyelids, face and back of the head, with the cancers usually disappearing within a matter of 2-3 weeks.

The cream also appeared to elicit an immune response (to have "memory") whereby newly appearing squamous cell carcinomas would disappear within a matter of days without requiring fresh application of the cream.

Some of the advantages of the composition for treating skin cancer (or its precursors) include that the composition specifically targets cancerous cells as opposed to surrounding healthy cells (unlike radiotherapy and chemotherapy), invasive surgical procedures (cancer removal using liquid nitrogen or surgical incision) can be avoided, and cancers on generally inoperable parts of the body can be treated (e.g. cancers on the lower eyelids).

Clearance of skin cancers and pre-cancerous growths were in some instances confirmed by biopsy by pathologists and medical practitioners. Some of those instances are described below.

Solar Keratosis Lesion

A punch specimen 3 mm in diameter and 2 mm in depth was taken of a lesion on a hand, and the specimen was embedded. Microscopic sections showed hyperkeratotic moderate to severely dysplastic solar keratosis in the punch specimen. Upon application of the cream twice daily for eight days, the lesion was confirmed by a doctor as having resolved.

Punch specimens 4 mm in diameter and 2 mm in depth were taken of lesions from a nose, and the specimens were embedded. Microscopic sections showed atrophic solar keratosis with patchy acantholytic bowenoid hypertrophic change. There was no evidence of invasive malignancy. Upon application of the cream twice daily for approximately 1 month, the lesions disappeared and

the punch incisions were only slightly visible.

Squamous Cell Carcinoma

A biopsy was taken of a lesion on a hand (a skin ellipse 7 x 2 x 2 mm with a slightly elevated cream area 2 mm). The biopsy showed the lesion to be an early well differentiated squamous cell carcinoma in skin with solar degeneration. Upon application of the cream twice daily for less than three weeks, the lesion was confirmed by a doctor as having resolved.

Example 3

Anti-Fungal Treatment

The cream as described in Example 1 has been proven effective for the treatment of fungal conditions, including athlete's foot and ringworm.

Although Whitfield's Ointment™ is commonly used to treat fungal infections, the cream of the present invention displayed superior antifungal activity over Whitfield's Ointment™ alone. It is believed that the sap works synergistically with one or more ingredients in the cream.

The cream was applied to the fungal infection twice a day. On average, tinea disappeared within 3-4 days. This result could not be achieved using Whitfield's Ointment™ alone.

Example 4

Anti-Viral Treatment

The cream as described in Example 1 has been proven effective for the treatment of sores, ulcers, lesions, blisters, cancers, inflammations and skin discolorations that are caused by a virus.

The cream was applied twice a day. The cream was used to effectively treat conditions caused by herpes simplex virus in the mouth and genital areas. The conditions cleared up within 2-3 weeks. The cream was also used to effectively treat carcinomas in genital areas caused by human papilloma virus. The carcinomas disappeared within 3 weeks.

Example 5

Treatment of Skin Defects and Other Conditions

The cream as described in Example 1 has been proven effective for the treatment of various skin defects and haemorrhoids. The cream has been used to treat eczema, dermatitis, brown age spots, moles, burns and seborrhoeic keratoses.

The cream was applied once or twice a day. Eczema, dermatitis and brown age spots cleared up or improved usually within about seven days. Haemorrhoids were effectively treated within 2-3 weeks. Seborrhoeic keratoses (maxillary area) were effectively treated within about three weeks. In one instance, brown age spots (on the backs of hands) faded after about four weeks. A growing dark brown mole (on the side of a nose) dropped off in less than three weeks, leaving smooth healthy skin with no scar tissue at all.

Throughout this specification, unless in the context of usage an alternative interpretation is required, the term "comprise" (and variants thereof such as "comprising" and "comprised") denotes the inclusion of a stated integer or integers but does not exclude the presence of another integer or other integers.

Whilst the above has been given by way of illustrative example of the invention, many modifications and variations may be made thereto by persons skilled in the art without departing from the broad scope and ambit of the invention as herein set forth.

Claims

1. A composition for preventing or treating skin cancer, said composition comprising an extract from a plant of the genus *Plumeria*.

2. The composition of claim 1, wherein the cancer or precursor of the cancer is selected from the group consisting of: squamous cell carcinoma; basal cell carcinoma; melanoma; Kaposi's sarcoma; cutaneous lymphoma; adnexal tumour; Merkel cell carcinoma; and solar keratosis.

3. A method for preventing or treating skin cancer in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

4. The method of claim 3, wherein the cancer or precursor of the cancer is selected from the group consisting of: squamous cell carcinoma; basal cell carcinoma; melanoma; Kaposi's sarcoma; cutaneous lymphoma; adnexal tumour; Merkel cell carcinoma; and solar keratosis.

5. The use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of skin cancer in a subject.

6. A composition for preventing or treating a fungal infection, said composition comprising an extract from a plant of the genus *Plumeria*.

7. The composition of claim 6, wherein the fungal infection is tinea.

8. The composition of claim 6 further comprising benzoic acid and salicylic acid.

9. A method for preventing or treating a fungal infection in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

10. The use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of a fungal infection in a subject.

11. A composition for preventing or treating a viral infection, said composition comprising an extract from a plant of the genus *Plumeria*.

12. The composition of claim 11, wherein the viral infection is due to a virus selected from the group consisting of: herpes simplex virus 1; herpes simplex virus 2; and human papillomavirus.

13. The composition of claim 11, wherein the composition is applied to a sore, ulcer, lesion, blister, cancer, inflammation, skin discoloration or other skin defect that is caused by a virus.

14. A method for preventing or treating a viral infection in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

15. The method of claim 14, wherein the viral infection is due to a virus selected from the group consisting of: herpes simplex virus 1; herpes simplex virus 2; and human papillomavirus.

16. The method of claim 14, wherein the composition is applied to a sore, ulcer, lesion, blister, cancer, inflammation, skin discoloration or other skin defect that is caused by a virus.

17. The use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for the prevention or treatment of a viral infection in a subject.

18. A composition for repairing or preventing a defect of the skin, said composition comprising an extract from a plant of the genus *Plumeria*.

19. The composition of claim 18, wherein the defect is selected from the group consisting of: an age spot; a benign tumour; a blister; a burn; chicken pox; a cold sore; a crack; cradle cap; dermatitis; diaper rash; eczema; a lesion; a mole; a papule; a pustule; a reddened area; rosacea; scaling; a stomatitis; an ulcer; a wound; and seborrhoeic keratosis.

20. A method of repairing or preventing a defect of the skin in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

21. The method of claim 20, wherein the defect is selected from the group consisting of: an age spot; a benign tumour; a blister; a burn; chicken pox; a cold sore; a crack; cradle cap; dermatitis; diaper rash; eczema; a lesion; a mole; a papule; a pustule; a reddened area; rosacea; scaling; a stomatitis; an ulcer; a wound; and seborrhoeic keratosis.

22. The use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for repairing or preventing a defect of the skin in a subject.

23. A composition for preventing or treating haemorrhoids, said composition comprising an extract from a plant of the genus *Plumeria*.

24. A method of preventing or treating haemorrhoids in a subject, said method comprising the step of administering to the subject a composition comprising an extract from a plant of the genus *Plumeria*.

25. The use of an extract from a plant of the genus *Plumeria* in the preparation of a medicament for preventing or treating haemorrhoids in a subject.

26. A therapeutic composition for topical use comprising an extract from a plant of the genus *Plumeria* and an organic base or emulsion base.

27. The therapeutic composition of claim 26, wherein the plant is a deciduous form of *Plumeria*.

28. The therapeutic composition of claim 26, wherein the extract comprises milky sap collected from the plant.

29. A method for preparing a therapeutic composition comprising an extract from a plant of the genus *Plumeria*, said method comprising the steps of:

collecting milky sap extract from the plant; and

combining the extract with an organic base or emulsion base.

30. The method of claim 29, wherein the extract is collected from an actively growing branch of the plant.

INTERNATIONAL SEARCH REPORT

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PCT/AU2005/001897

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

A61K 36/24 (2006.01) ***A61P 31/10*** (2006.01) ***A61P 35/00*** (2006.01)
A61P 17/00 (2006.01) ***A61P 31/12*** (2006.01)
A61P 17/02 (2006.01) ***A61P 31/22*** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS, DERWENT (plumeria, frangipani, herpes, viral infection, cancer, carcinoma, tumour, skin)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GEVARA, A. P., *et al.*, Antimutagens from *Plumeria acuminata* Ait., Mutation Research, (1996), vol. 361 (no. 2-3), pages 67-72 (see entire document, in particular page 67 column 2 lines 1-4 and page 71)	1-5, 18-22
X	TAN, G. T., *et al.*, Evaluation of natural products as inhibitors of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase, J. Natural Products (1991), vol. 54 (no. 1), pages 143-154 (see entire document, in particular page 145 lines 35 to 45, page 149 line 30, page 150 line 11 and page 153 lines 25 to 32)	11, 13-14, 16-17
X	KARDONO, L. B., *et al.*, Cytotoxic constituents of the bark of Plumeria rubra collected in Indonesia, J. Natural Products (1990), vol. 53, (no. 6), pages 1447-1455 (see entire document, in particular page 1451 Table 3 column B, page 1452 lines 28-30)	1-5

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"O" document referring to an oral disclosure, use, exhibition or other means
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 January 2006	7 FEB 2006
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer **NORMAN BLOM** Telephone No : (02) 6283

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2005/001897

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAMBURGER, M. O., *et al.*, Traditional medicinal plants of Thailand. XVII. Biologically active constituents of Plumeria rubra, J. Ethnopharmacology (1991), vol. 33 (no. 3), pages 289-292 (see the entire document, in particular the disclosure contained on page 289)	6, 9-11, 14, 17
X	Workers Online, Issue No 66, 11 August 2000 (online), (retrieved on 5 January 2006). Retrieved from the internet <URL: http://workers.labor.net.au/66/b_tradeunion_nurse.html>. This document first captured by the internet archive [waybackmachine] on 19 August 2000. (see the passage relating to treatment of herpes zoster with sap of frangipani tree)	11, 13-14, 16-17
X	The Herpes News MARCH 1999 The Herpes News Archive (online) (retrieved on 4 January 2006). Retrieved from the internet <URL: http://www.racoon.com/theherpesnews/99MAR.htm>. This document was first captured by the internet archive [waybackmachine] on 10 January 2001 (see paragraph beginning "25 – The Herpes Garden – Frangipani..")	11-22
X	Derwent abstract accession number 2000-365980/32, Class B04, BR 9705331 A (DINIZ BUENO E) 18 April 2000 (see the entire abstract)	18-22, 26
X	Derwent abstract accession number 2002-029792/04, Class B04 D21, JP 2001261544 A (Tanabe Seiyaku Co.) 26 September 2001 (see the entire abstract	18-22
X	Derwent abstract accession number 2002-646987/70, Class B04 D21, JP 2002097151 A (Maruzen Seiyaku KK) 2 April 2002 (see the entire abstract)	18-22, 26-27
P,X	Derwent abstract accession number 2005-649462/66, Class B04, WO 2005087246 A1 (NEROME K) 22 September 2005 (see the entire abstract)	1-5
P, X	EP 1527783 A1 (Health Research Inc.) 4 May 2005 (see in particular paragraphs [0004],[0005], [0014], [0017]-[0018], [0023]-[0027])	1-5
X	US 2002/0182272 A1 (HALSTEAD, Bruce) 5 December 2002 (see in particular paragraphs [0003], [0005] and claim 10)	1-6, 9-18
X	LEVEN, M. *et al.*, Screening of higher plants for biological activities I. Antimicrobial Activity, PLANTA MEDICA (1979), vol. 36, pp. 311-321 (see in particular page 312 column 2 "test organisms", page 317 Table 1 entry 85 and page 320 column 1)	6-7, 9-10
X	VAN DEN BERGHE, D. A., *et al.*, Screening of Higher Plants For Biological Activities. II. Antiviral activity, LLOYDIA (1978), vol. 41, No. 5, pp.463-471 (see in particular page 465 Table I entry 18 and page 469 last three lines and page 470 first line)	11, 14, 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2005/001897

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STICHER, O., Plant Mono-, Di-, and Sesquiterpenoids with Pharmacological or Therapeutical Activity. In WAGNER, H. and WOLFF, P. (Eds.), New Natural Products with Pharmacological, Biological or Therapeutical Activity (1977) SPRINGER VERLANG, Berlin, pages 137-176 (see in particular page 148 lines 16-28 and page 149)	6, 9-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU2005/001897

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
BR	9705331	NONE					
JP	2001261544	NONE					
JP	2002097151	NONE					
WO	2005087246	JP	2005289963				
EP	1527783	US	2005222053				
US	2002182272	AU	2003238842	EP	1551419	US	2002182217
		US	2002182227	US	2002187957	US	2003083226
		US	2005129780	WO	03101389	WO	2004105701

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX